

# PATENT COOPERATION TREATY

## PCT


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### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

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|---|--|--|--|--|
| Applicant's or agent's file reference<br>M/45173-PCT  |  | <b>FOR FURTHER ACTION</b>  |  | See Form PCT/IPEA/416                        |
| International application No.<br>PCT/EP2004/008207  |  | International filing date (day/month/year)<br>22.07.2004                 |  | Priority date (day/month/year)<br>24.07.2003 |
| International Patent Classification (IPC) or national classification and IPC<br>C07D487/04, A61K31/519, A61P25/22   |  |  |  |  |
| Applicant<br>FERRER INTERNACIONAL S.A. et al.   |  |  |  |  |
| <p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> |  |  |  |  |
| <p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>   |  |  |  |  |
| Date of submission of the demand<br><br>05.01.2005  |  | Date of completion of this report<br><br>24.06.2005                      |  |  |
| Name and mailing address of the international preliminary examining authority:<br> European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465   |  | Authorized Officer<br><br>Wörth, C<br><br>Telephone No. +49 89 2399-8726 |  |  |



**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2004/008207

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**Box No. I Basis of the report**

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1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

**Description, Pages**

1-55 as originally filed

**Claims, Numbers**

1-36 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,  
☒ claims Nos. 22-32 with respect to IA

because:

- ☒ the said international application, or the said claims Nos. 22-32 with respect to IA relate to the following subject matter which does not require an international preliminary examination (specify):

**see separate sheet**

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- ☐ has not been furnished  
☐ does not comply with the standard

the computer readable form

- ☐ has not been furnished  
☐ does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT  
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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

|                               |             |                 |
|-------------------------------|-------------|-----------------|
| Novelty (N)                   | Yes: Claims | 1-36            |
|                               | No: Claims  |                 |
| Inventive step (IS)           | Yes: Claims | 1-36            |
|                               | No: Claims  |                 |
| Industrial applicability (IA) | Yes: Claims |                 |
|                               | No: Claims  | Yes: 1-21,33-36 |

2. Citations and explanations (Rule 70.7):

**see separate sheet**

**1. Re Item I (*Basis of the report*)**

Reference is made to the following documents:

- D1: EP-A-0 264 773 (AMERICAN CYANAMID CO) 27 April 1988 (1988-04-27)
- D2: US-A-5 538 977 (DUSZA JOHN P ET AL) 23 July 1996 (1996-07-23)
- D3: DE 43 33 705 A (EGE GUENTER PROF DR) 6 April 1995 (1995-04-06)
- D4: GB-A-1 412 017 (ICN PHARMACEUTICALS) 29 October 1975 (1975-10-29)
- D5: DE 101 53 344 A (GRUENENTHAL GMBH ; UNIVERSITEIT LEIDEN LEIDEN (NL)) 15 May 2003 (2003-05-15)
- D6: WO 00/59908 A (DU PONT PHARM CO) 12 October 2000 (2000-10-12)

**2. Re Item III (*Non-establishment of opinion with regard to novelty, inventive step and industrial applicability*)**

Claims 22-32 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**3. Re Item V (*Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement*)**

**3.1 Subject-matter**

The present application relates to certain pyrazolo[1,5-a]pyrimidines characterized by a nitro-group at position 3. The claimed compounds exhibit affinity for GABA $\alpha$  receptor thereby being useful for the treatment of inter alia anxiety and sleep disorders.

**3.2 Novelty**

The subject-matter of claim 1 differs from

- D1-D3 in view of the present **nitro-group** at position 3 of the pyrazolo[1,5-

- D4 a]pyrimidine moiety  
in view of present R<sub>1</sub> being an aromatic moiety (see definition of  
corresponding R<sub>2</sub> in D4)
- D5-D6 in view of the present **nitro-group** at position 3 of the pyrazolo[1,5-  
a]pyrimidine moiety.

***The requirements of Art. 33(2) PCT are fulfilled.***

### 3.3 Inventive step

Document D2 is considered as closest prior art. This document discloses pyrazolo[1,5-a]pyrimidines substituted at position 3 and 7 having anxiolytic, anti-convulsant, sedative-hypnotic and skeletal relaxant activity.

In view of this document, the problem to be solved can be regarded as the provision of further compounds having the same activity.

The solution provided consists in compounds according to present claim 1 characterized by a nitro-group at position 3 of the pyrazolo[1,5-a]pyrimidine core.

The problem is considered as being solved in view of the pharmacological data on pages 17-21 of the specification.

The provided solution is presently considered as involving an inventive step. Although documents D1-D3 already disclose a variety of suitable substituents (from hydrogen to aromatic substituents) at position 3 of the pyrazolo[1,5-a]pyrimidine core, the comparative tests vis-à-vis zaleplon, which differs only in the substituent at position 3, indicate a surprisingly superior activity of the claimed compounds.

***The requirements of Art. 33(3) PCT are fulfilled.***

### 3.4 Industrial applicability

For the assessment of the present claims 25-32 on the question whether they are

industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

### **3.5 Certain observations**

As far as the subject-matter of claims 22-24, 34 and 35 is concerned it is stressed that the selective occupation of a receptor cannot be considered in itself as a therapeutic application. The discovery, that a substance binds a receptor still needs to find an (unexpected) practical application in the form of a defined real treatment of any pathological condition to be considered as an invention eligible for patent protection.